Amendments

Claims 104, 112, and 119 are amended solely to correct punctuation, so that the elements of the Markush group are all similarly separated (see, Specification as filed, p.4, lines 17-19) and by commas. This amendment introduces no new matter. A petition to rescind the finality of the subject Action is submitted herewith; hence, these amendments are submitted to be enterable as a matter of right.

I. CLAIMS 68-91 AND 93-119 ARE PATENTABLE UNDER 35USC101 (UTILITY)

Claim 68-91 AND 93-119 relate to diagnostic probes that specifically detect Robo proteins or transcripts. Robo proteins comprise a key component of the body's nerve cell guidance system. In particular, the inventors disclose that Robo functions as the critical gatekeeper controlling midline crossing of spinal axons (Specification, p.2, line 28 - p.3, line 2). These neural guidance molecules provide for proper enervation during development, but also prevent regeneration of proper nerve pathways following spinal injuries in adults. Hence, Robo polypeptides are important targets for therapeutic intervention (e.g. Specification, p.13, line 28 - p.14, line 20) and the ability to trace the presence of Robo in spinal tissue (e.g. p.29, lines 16-17; p.14, line 30 - p.17, line 18; p.20, line 30 - p.21, line 6; p.29, lines 14-16; p.31, lines 30-31; p.34, line 22 - p.35, line 4; etc.) is critical to developing therapy for spinal injuries.

The claims are limited to particularly useful diagnostic probes. The polynucleotides of claims 68, 79, 88, 100 and 112 (and their dependencies) encode polypeptides which elicit a corresponding Robo-specific antibody probe. As taught by our Specification (supra), these probes are useful to trace the presence of Robo expression in tissue. The polynucleotides of claims 75, 85, 96, 108 and 118 (and their dependencies) provide specific hybridization probes for the corresponding Robo-1 mRNA. As taught by our Specification (supra), these probes are useful to trace the presence of Robo expression in tissue.

The Action misconstrues the claims to require that the reagents serve to diagnose or treat disease. No such requirement is present in the claims. As repeatedly used in the Specification, the probes are diagnostic of the presence of Robo transcripts and protein; e.g. p.3, lines 12-13. These probes are as industrially useful as any equipment or reagents used in commercial research. For example, specific antibodies diagnostic of the presence of nerve guidance molecules are commercially bought, sold and licensed. Appended are product data sheets from Santa Cruz Biotechnology, Inc., and the Development Studies Hybridoma Bank documenting present, real-world, industrial commerce (buying and selling) of probes for natural nerve guidance molecules, including three different anti-Robo antibody reagents. Unlike the invention in Brenner v. Manson, here the record documents a present, real-world commercial market for the invention.

II. CLAIMS 68-91 AND 93-119 ARE PATENTABLE UNDER 35USC112, FIRST PARAGRAPH (ENABLEMENT)

Claims 68-91 and 93-119 are supported by a specific and substantial, credible asserted utility, supra, and hence, one skilled in the art would clearly know how to use the claimed invention. In fact, use of Robo-specific probes as claimed is expressly described, e.g. p.29, lines 14-16 and 16-17. The invention defines commercially useful subject matter (supra) and the Specification shows one skilled in the art knows how to use the claimed invention (supra).

III. CLAIMS 81, 100, 102-104 AND113-114 ARE PATENTABLE UNDER 35USC112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

Claims 81, 100, 102-104, 113-114 are supported by a proper written description; in particular:

The polypeptide defined by residues 1-942 of SEQ ID NO:4 was separately disclosed in Table 1 as filed. That we provided an alignment of this polypeptide with other robo family members does not diminish the fact that is separately disclosed. Furthermore, the Specification teaches that the polypeptides of the invention include incomplete translates and deletion mutants of SEQ ID NO:4 (p.4, lines 6-8). In fact, this particularly disclosed polypeptide defines a robo domain (extracelluar domain) taught to be advantageously specifically targeted with monoclonal antibodies (p.29, lines 16-17).

The polypeptide defined by residues 68-259 of SEQ ID NO:8 was separately disclosed on p.4, line 19 of the Specification as filed.

The polypeptide defined by residues 1-284 of SEQ ID NO:10 was separately disclosed in Table 1 as filed. That we provided an alignment of this polypeptide with other robo family members does not diminish the fact that is separately disclosed. Furthermore, the Specification teaches that the polypeptides of the invention include incomplete translates and deletion mutants of SEQ ID NO:10 (p.4, lines 6-8).

IV. CLAIMS 88-90 ARE PATENTABLE UNDER 35USC102(a)

Claims 88-90 are free of the cited art. The Sptrembl-11 seq. O01632 was made of record by the present Examiner in her Action mailed 1/21/00; on the accompanying PTO-892 she indicated for this sequence a date of 7/1/97, and the accompanying sequence printout indicated a record creation date of 7/1/97, and a last annotation update date of 11/1/98. In addition, someone from the PTO handwrote on the record printout next to the 7/1/98 creation date, "Public availability date".

As we have previously explained, O01632 is identical in sequence to EMBL/GenBank amino acid entry 1825710, which was generated and submitted by the same authors, but was reportedly released earlier, on Apr 21, 1997. 1825710 (and O01632) appear to encode residues 424-1297 of our SEQ ID NO:6.

Also on Apr 21, 1997, Genbank reportedly released U88183 and 1825711. U88183 (which we made of record in our Response transmitted on 2/7/00) is the sequence of X chromosome cosmid ZK377 and its annotation includes predicted open reading frames, including

1825710 and 1825711. 1825711 appears to encode residues 1-423 of SEQ ID NO:6. Hence, the sequence of natural C. elegans robo (SEQ ID NO:6, also known as sax-3, see p.28, line 2 of our specification) comprises a recombination of 1825710 and 1825711. Note that the annotation reference to the Wilson (1994) publication describing a chromosome III cosmid is not for any X chromosome sequence, but merely for methods used to sequence large parts of C. elegans chromosomes.

To the extent that the sequences of the 1825710 and 1825711 predicted reading frames are citeable art under 35USC102(a), our Supplemental Declaration under 37CFR1.131 (made of record with our Response mailed Aug 31, 2000) demonstrates that Applicants had possession of the claimed subject matter prior to their publication. Specifically, the Declaration shows that the full-length sequence encoding C. elegans robo (SEQ ID NO:6) was determined by Applicants prior to the April 21, 1997 publication dates of 1825710 and 1825711.

The present Action makes numerous inaccurate representations and appends what appears to be a printout of an electronic record relating to U88183. First, we did not make any of the admissions alleged by the Examiner and respectfully request that if she wishes to rely on our statements in the record, she quote them accurately and completely. Second, the creation date of an EMBL or GenBank record is not the public availability date. The creation date is the date the record was originally created. Frequently, these records are maintained in secrecy until a predetermined publication or patent filing date is effected. Furthermore, the creation date does not often reflect the record as subsequently accessed. Like most electronic databases, Genbank and EMBL are constantly updating, amending, annotating and otherwise supplementing their records. These newer "editions" retain the creation date of the original record, but were obviously not in existence at that date. Here, the Examiner seeks to rely on a creation date for a record that could not logically have existed on that creation date. A document (electronic or otherwise) that makes explicit reference to dates and events in Apr 1997 and Mar 2000 could not logically have been "published" or made "publically available" in Feb 1997. This rejection is akin to citing a year 2002-updated article in the Encyclopedia Brittanica and relying on the encyclopedia's year 1768 original publication date.

Highlighted copies of EMBL and GenBank database information for submitters (including information on withholding public availability of records after submission and record creation) is attached. Also attached is a Sample GenBank Record explaining that even the date of last modification may not correspond to the release date (p.6).

V. CLAIMS 108-110 ARE PATENTABLE UNDER 35USC102(a)

Claims 108-110 are free of the cited art. As noted in our Second Declaration under 37CFR1.131 (filed with our Response mailed 8/31/00) the Word document appended thereto describes a cDNA sequence including the 5' UTR of Human Robo1 (bases 1-509) and Human Robo1 coding sequence (bases 510-5366) encoding amino acids 1-1619 of Human Robo 1. Claims 108-100 are limited to polynucleotide sequences within this cDNA; hence, Applicants

have documented possession of the invention as claimed prior to the purported publication date of the GenBank Accession No. Z95705.

More particularly, claims 108-110 encompass polynucleotides comprising a sequence falling within the bounds of SEQ ID NO:7, nucleotides 134-3630. This sequence is identical to the sequence bound by nucleotides 643-4139 as shown in the cited Word document; in fact, nucleotides 1-4856 of SEQ ID NO:7 are identical to nucleotides 510-5365 as shown in the cited Word document. A marked up copy of the Word document, showing the boundaries corresponding to SEQ ID NO:7, nucleotides 1-4856 and 134-3630 is attached.

VI. CLAIMS 94-95 ARE PATENTABLE UNDER 35USC103(a)

Claims 94-95 are free of the cited art because the GenBank Accession No. O01632 (U88183) upon which the Action principally relies is not prior art for the reasons explained above.

The Examiner is invited to call the undersigned if she would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

We hereby petition for and authorize charging to our Deposit Account No. 19-0750 all necessary extensions of time. The Commissioner is hereby authorized to charge any fees or credit any overcharges relating to this communication to our Deposit Account No. 19-0750 (order. B98-006-2).

Respectfully submitted,
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encl. Product data sheets, Sant Cruz Biotechnology Inc. (16p)
Product data sheets, Development Studies Hybridoma Bank (3p)
EMBL database information (7p)
GenBank database information (5p)
Sample GenBank Record (17p)
Marked up Word document (2p)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

104. (Amended) An isolated polynucleotide according to claim 100, wherein the sequence is selected from the group consisting of residues 1-167, 68-259, 1-67 joined to 168-259[;], and 1-67 joined to 260-451 of SEQ ID NO:8.

112. (Amended) An isolated polynucleotide comprising a coding strand encoding a polypeptide comprising a sequence selected from the group consisting of residues 5-16, 38-47, 83-94, 112-125, 168-180, 195-209, 222-235[;], and 241-254 of SEQ ID NO:10, wherein the polypeptide elicits a human Robo-2 (SEQ ID NO:10) specific antibody.

119. (Amended) An isolated polynucleotide according to claim 118, wherein the sequence is selected from the group consisting of nucleotides 1-273[;], 274-558[;], and 559-854 of SEQ ID NO:9.